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| (21) International Application Number: PCT/US95/01090 (22) International Filing Date: 23 January 1995 (23.01.95) (30) Priority Data: 08/184,813 21 January 1994 (21.01.94) US (71) Applicant: BAXTER INTERNATIONAL INC. [US/US]; One Baxter Parkway, Deerfield, IL 60015 (US). (72) Inventors: MARTIS, Leo; 5524 Old Wood Court, Long Grove, IL 60047 (US). BURKE, Ron; 2914 N. Mitchell, Arlington Heights, IL 60004 (US). SHOCKLEY, Ty; 1236 Cavell Avenue, Highland Park, IL 60035 (US). HENDERSON, Lee, W.; 725 N. Sheridan Road, Lake Forest, IL 60045 (US). FALLER, Bernardette; 11, route de Rouffach, F-68000 Colmar (FR). (74) Agents: BORECKI, Thomas, S. et al.; 1620 North Waukegan Road, McGaw Park, IL 60085 (US). | (81) Designated States: AU, BR, CA, CN, JP, KR, MX, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> | |
| (54) Title: PERITONEAL DIALYSIS SOLUTIONS CONTAINING MALTODEXTRINS AND AMINO ACIDS (57) Abstract <p>A peritoneal dialysis solution comprising as osmotic agents approximately 2.0 to about 6.0 % (w/v) maltodextrins and approximately 0.25 to about 2.0 % (w/v) amino acids. The peritoneal dialysis solution will also include other components such as sodium, chloride, lactate, bicarbonate, calcium, and magnesium.</p> | | |

- 24 -

WE CLAIM:

1. A peritoneal dialysis solution comprising as osmotic agents:

approximately 2.0 to about 6.0% (w/v) maltodextrins;
5 and

approximately 0.25 to about 2.0% (w/v) amino acids.

2. The peritoneal dialysis solution of Claim 1 wherein the amino acids comprise both essential and non-essential amino acids.

10 3. The peritoneal dialysis solution of Claim 1 including sodium, chloride, lactate, bicarbonate, calcium, and magnesium.

4. The peritoneal dialysis solution of Claim 1 wherein the solution includes:

15 120 to about 140 (mEq/L) sodium;
70 to about 110 (mEq/L) chloride;
0 to about 45.00 (mEq/L) of lactate;
0 to about 45.00 (mEq/L) of bicarbonate;
0 to about 4.00 (mEq/L) of calcium; and
20 0 to about 4.00 (mEq/L) of magnesium.

5. The peritoneal dialysis solution of Claim 1 wherein the pH of the solution is approximately 6.0 to 7.4.

25 6. The peritoneal dialysis solution of Claim 1 wherein the maltodextrins have the following composition:

| | |
|------------------------------|-------------------------|
| Weight Average Mol. Wt. (Mw) | 10,000 - 16,000 daltons |
| Number Average Mol. Wt. (Mn) | 4,000 - 8,000 daltons |
| Polydispersity | 1.0 - 4.0 |
| Fraction > 100,000 daltons | NMT 1.0% |
| 30 Mono, Di, Trisaccharides | NMT 5.0% |
| Distribution | normal |
| Alpha (1-4) | NLT 90% |
| Aluminum (10% solution) | <10ppb |

- 25 -

| | |
|-------------------------------|---------------|
| Aqueous Solubility | NLT 10% (w/v) |
| pH (10% solution) | 5.0 - 7.0 |
| Heavy Metals | <5ppm |
| DP (Degree of polymerization) | |
| 5 greater than 20 | ≥ 75% |
| DP greater than 50 | ≥ 50% |
| DP greater than 100 | ≥ 25% |

7. The peritoneal dialysis solution of Claim 1 wherein the maltodextrins are derived from the hydrolysis of starch.

8. The peritoneal dialysis solution of Claim 1 wherein the amino acids comprise:

| | <u>Amino Acid</u> | <u>Conc. (mg%)</u> |
|----|-------------------|--------------------|
| | Leucine | 74 - 112 |
| 15 | Valine | 100 - 151 |
| | Threonine | 47 - 71 |
| | Isoleucine | 61 - 92 |
| | Lysine.HCl | 55 - 83 |
| | Histidine | 52 - 78 |
| 20 | Methionine | 32 - 48 |
| | Phenylalanine | 42 - 62 |
| | Tryptophan | 20 - 30 |
| | Alanine | 68 - 103 |
| | Proline | 43 - 65 |
| 25 | Arginine | 60 - 113 |
| | Glycine | 36 - 55 |
| | Serine | 48 - 72 |
| | Tyrosine | 20 - 35 |
| | Aspartate | 55 - 83 |
| 30 | Glutamate | 55 - 83 |

9. The peritoneal dialysis solution of Claim 1 wherein the amino acids are chosen so as to have the following ratios:

- 26 -

| | |
|------------------------|-----------|
| Phenylalanine/Tyrosine | 1.3 - 3.0 |
|------------------------|-----------|

| | |
|-----------------------------|-----------|
| Essential/Total Amino Acids | 0.4 - 0.7 |
|-----------------------------|-----------|

10. The peritoneal dialysis solution of Claim 1 wherein maltodextrins and amino acids comprise the only osmotic agents.

11. A peritoneal dialysis solution comprising:

| | |
|-----------------------|------------|
| Maltodextrins (% w/v) | 2.0 - 6.0 |
| Amino Acids (% w/v) | 0.25 - 2.0 |
| Sodium (mEq/L) | 120 - 140 |
| Chloride (mEq/L) | 70 - 110 |
| Lactate (mEq/L) | 0.0 - 45.0 |
| Bicarbonate (mEq/L) | 0.0 - 45.0 |
| Calcium (mEq/L) | 0.0 - 4.0 |
| Magnesium (mEq/L) | 0.0 - 4.0 |
| pH | 6.0 - 7.4 |

12. The peritoneal dialysis solution of Claim 11 wherein the maltodextrins are derived from the hydrolysis of starch and have the following composition:

| | |
|-------------------------------|-------------------------|
| Weight Average Mol. Wt. (Mw) | 10,000 - 16,000 daltons |
| Number Average Mol. Wt. (Mn) | 4,000 - 8,000 daltons |
| Polydispersity | 1.0 - 4.0 |
| Fraction > 100,000 daltons | NMT 1.0% |
| Mono, Di, Trisaccharides | NMT 5.0% |
| Distribution | normal |
| Alpha (1-4) | NLT 90% |
| Aluminum (10% solution) | <10ppb |
| Aqueous Solubility | NLT 10% (w/v) |
| pH (10% solution) | 5.0 - 7.0 |
| Heavy Metals | <5ppm |
| DP (Degree of polymerization) | |
| greater than 20 | ≥ 75% |
| DP greater than 40 | ≥ 50% |
| DP greater than 80 | ≥ 25% |

- 27 -

13. The peritoneal dialysis solution of Claim 11 wherein the amino acids comprise:

| | <u>Amino Acid</u> | <u>Conc. (mg%)</u> |
|----|-------------------|--------------------|
| | Leucine | 74 - 112 |
| 5 | Valine | 100 - 151 |
| | Threonine | 47 - 71 |
| | Isoleucine | 61 - 92 |
| | Lysine.HCl | 55 - 83 |
| | Histidine | 52 - 78 |
| 10 | Methionine | 32 - 48 |
| | Phenylalanine | 42 - 62 |
| | Tryptophan | 20 - 30 |
| | Alanine | 68 - 103 |
| | Proline | 43 - 65 |
| 15 | Arginine | 60 - 113 |
| | Glycine | 36 - 55 |
| | Serine | 48 - 72 |
| | Tyrosine | 20 - 35 |
| | Aspartate | 55 - 83 |
| 20 | Glutamate | 55 - 83 |

14. The peritoneal dialysis solution of Claim 11 wherein the amino acids are chosen so as to have the following ratios:

| | | |
|----|-----------------------------|-----------|
| | Phenylalanine/Tyrosine | 1.3 - 3.0 |
| 25 | Essential/Total Amino Acids | 0.4 - 0.7 |

15. The peritoneal dialysis solution of Claim 11 wherein maltodextrins and amino acids comprise the only osmotic agents.

16. A method for providing an osmotic agent for a peritoneal dialysis solution comprising the steps of selecting as the osmotic agent two compositions, one having a molecular weight equal to or greater than 10,000 daltons and comprising approximately 2.0 to about 6.0%

- 28 -

(w/v) of the composition and a second composition having a molecular weight equal to or less than 300 daltons and comprising approximately .25 to about 2.0% w/v of the composition.

5 17. The method of Claim 16 wherein the osmotic agent includes maltodextrin and amino acids.

18. The method of Claim 17 wherein the maltodextrins are derived from the hydrolysis of starch and have the following composition:

| | | |
|----|-------------------------------|-------------------------|
| 10 | Weight Average Mol. Wt. (Mw) | 10,000 - 16,000 daltons |
| | Number Average Mol. Wt. (Mn) | 4,000 - 8,000 daltons |
| | Polydispersity | 1.0 - 4.0 |
| | Fraction > 100,000 daltons | NMT 1.0% |
| | Mono, Di, Trisaccharides | NMT 5.0% |
| 15 | Distribution | normal |
| | Alpha (1-4) | NLT 90% |
| | Aluminum (10% solution) | <10ppb |
| | Aqueous Solubility | NLT 10% (w/v) |
| | pH (10% solution) | 5.0 - 7.0 |
| 20 | Heavy Metals | <5ppm |
| | DP (Degree of polymerization) | |
| | greater than 20 | ≥ 75% |
| | DP greater than 50 | ≥ 50% |
| | DP greater than 100 | ≥ 25% |

25 19. The method of Claim 17 wherein the amino acids comprise:

| | | |
|----|-------------------|--------------------|
| | <u>Amino Acid</u> | <u>Conc. (mg%)</u> |
| | Leucine | 74 - 112 |
| | Valine | 100 - 151 |
| 30 | Threonine | 47 - 71 |
| | Isoleucine | 61 - 92 |
| | Lysine.HCl | 55 - 83 |
| | Histidine | 52 - 78 |

- 29 -

| | | |
|----|---------------|----------|
| | Methionine | 32 - 48 |
| | Phenylalanine | 42 - 62 |
| | Tryptophan | 20 - 30 |
| | Alanine | 68 - 103 |
| 5 | Proline | 43 - 65 |
| | Arginine | 60 - 113 |
| | Glycine | 36 - 55 |
| | Serine | 48 - 72 |
| | Tyrosine | 20 - 35 |
| 10 | Aspartate | 55 - 83 |
| | Glutamate | 55 - 83 |

20. A two part peritoneal dialysis solution designed to be mixed prior to infusion into a patient comprising:

15 a first part housed in a first structure including approximately 2.0 to about 6.0% (w/v) maltodextrin and a pH of approximately 4.0 to about 5.5;

a second part housed in a second structure including amino acids; and

20 including in either the first or the second structure a sufficient amount of the following ingredients so when the first part and second part are mixed the following is provided: 120 to about 140 (mEq/L) sodium; 70.0 to about 110.00 (mEq/L) chloride;
 25 0.0 to about 5.0 (mEq/L) lactate; 0.0 to about 45.0 (mEq/L) bicarbonate; 0.0 to about 4.0 mEq/L calcium; and 0.0 to about 4.0 (mEq/L) magnesium.

21. The two part peritoneal dialysis solution of Claim 20 wherein the first and second structures are two
 30 separate chambers of a single container.

- 30 -

22. The two part peritoneal dialysis solution of Claim 20 wherein the pH of a resultant solution, comprising a mixture of the first part and the second part, is approximately 6.0 to about 7.4.